

Using the underlying anatomy to infer white-matter pathways and vice versa

Anastasia Yendiki

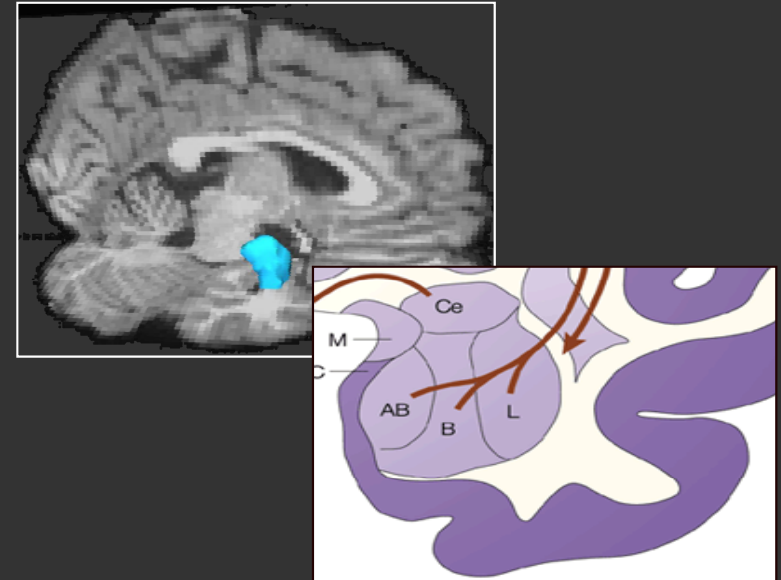


HMS/MGH/MIT Athinoula A. Martinos Center for
Biomedical Imaging

Tract-based amygdala segmentation

Work by Zeynep Saygin [zsaygin@mit.edu]

- Amygdala is important in
 - Fear conditioning
 - Emotional evaluation
 - Stimulus reappraisal
- Implicated in numerous pathologies
 - Depression
 - Anxiety disorders
 - Bipolar disorder
 - Autism
- Four nuclei with distinct functions described in animal studies
 - Central
 - Lateral
 - Basal & Accessory Basal
 - Medial
- Normal and pathological roles of nuclei unknown in humans

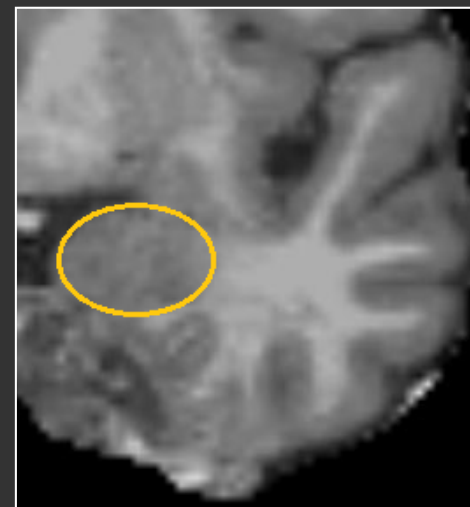


Baxter & Murray 2002

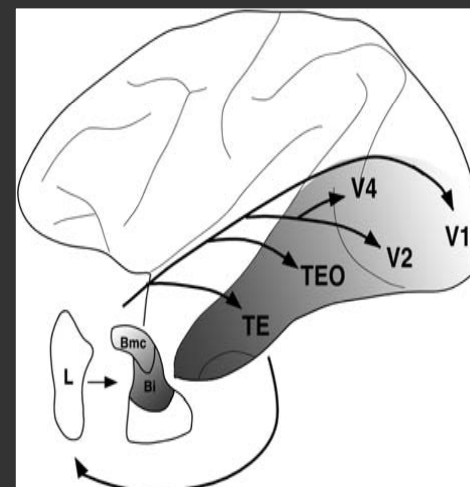
Amygdaloid nuclei in MRI

Work by Zeynep Saygin [zsaygin@mit.edu]

- Structural MRI:
 - Structural scan resolution and SNR too low to distinguish nuclei
 - fMRI studies limited to averaging over entire amygdala
- Distinct but highly overlapping patterns of connectivity
 - Lateral and basal nuclei differentiated from central and medial by connectivity to visual areas
 - This is not enough to separate basal from lateral
- Connectivity patterns can be used to segment amygdala into nuclei



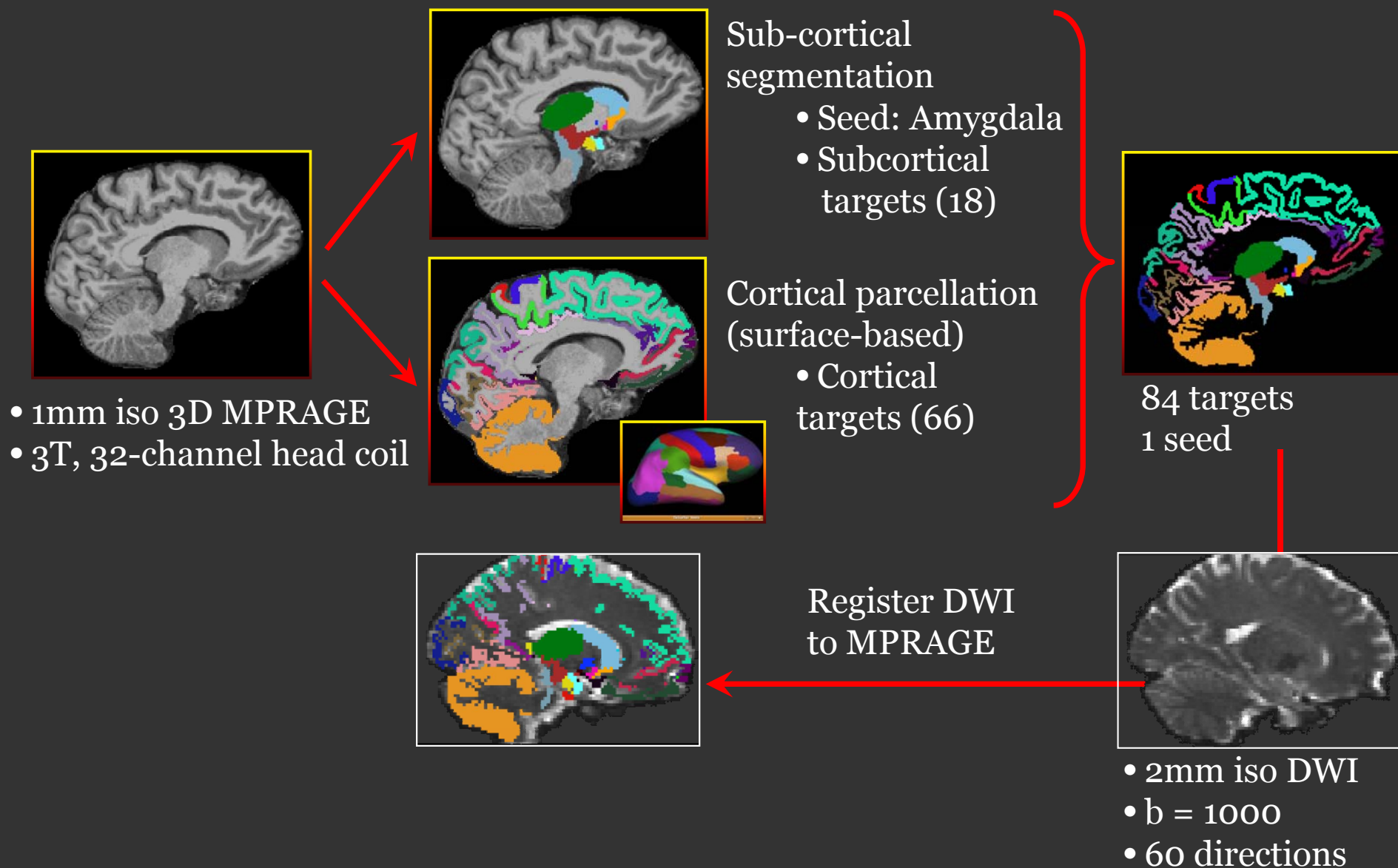
1mm³ structural scan



Freese & Amaral 2005

Step 1: Anatomical ROIs

Work by Zeynep Saygin [zsaygin@mit.edu]



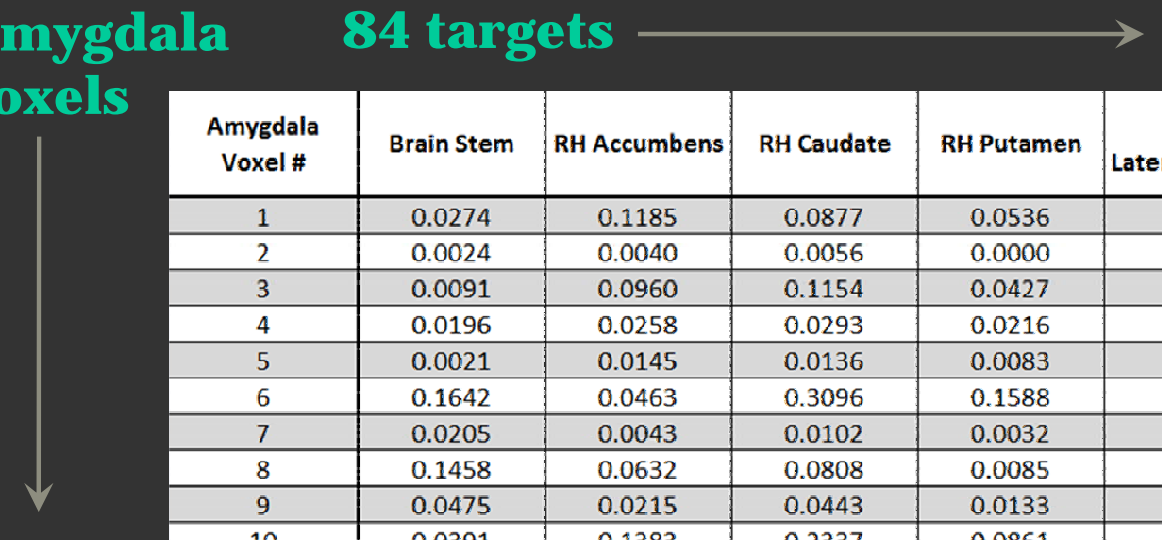
Step 2: Probabilistic tractography

Work by Zeynep Saygin [zsaygin@mit.edu]

- Calculate connection probability from each voxel in the amygdala to each target ROI

**Amygdala
voxels**

84 targets



Amygdala Voxel #	Brain Stem	RH Accumbens	RH Caudate	RH Putamen	RH Lateralorbitofrontal	RH Parahippocampal	RH Superiorfront
1	0.0274	0.1185	0.0877	0.0536	0.7915	0.0446	0.0192
2	0.0024	0.0040	0.0056	0.0000	0.0377	0.1293	0.0000
3	0.0091	0.0960	0.1154	0.0427	0.7338	0.0129	0.0142
4	0.0196	0.0258	0.0293	0.0216	0.3101	0.1956	0.0000
5	0.0021	0.0145	0.0136	0.0083	0.1165	0.1214	0.0000
6	0.1642	0.0463	0.3096	0.1588	0.9952	0.0119	0.1077
7	0.0205	0.0043	0.0102	0.0032	0.0919	0.0108	0.0000
8	0.1458	0.0632	0.0808	0.0085	0.0761	0.0000	0.0406
9	0.0475	0.0215	0.0443	0.0133	0.2313	0.0086	0.0060
10	0.0391	0.1383	0.2337	0.0861	0.9736	0.0029	0.0360
11	0.0091	0.0293	0.0366	0.0129	0.8899	0.0003	0.0025
12	0.0031	0.0072	0.0073	0.0050	0.1411	0.0053	0.0015
13	0.1609	0.0196	0.0425	0.0245	0.2371	0.0000	0.0000
14	0.0188	0.1029	0.1106	0.0921	0.6792	0.0418	0.0161
15	0.0300	0.0331	0.0375	0.0117	0.0650	0.0250	0.0000

- Threshold and binarize probability values

Step 3: Classification

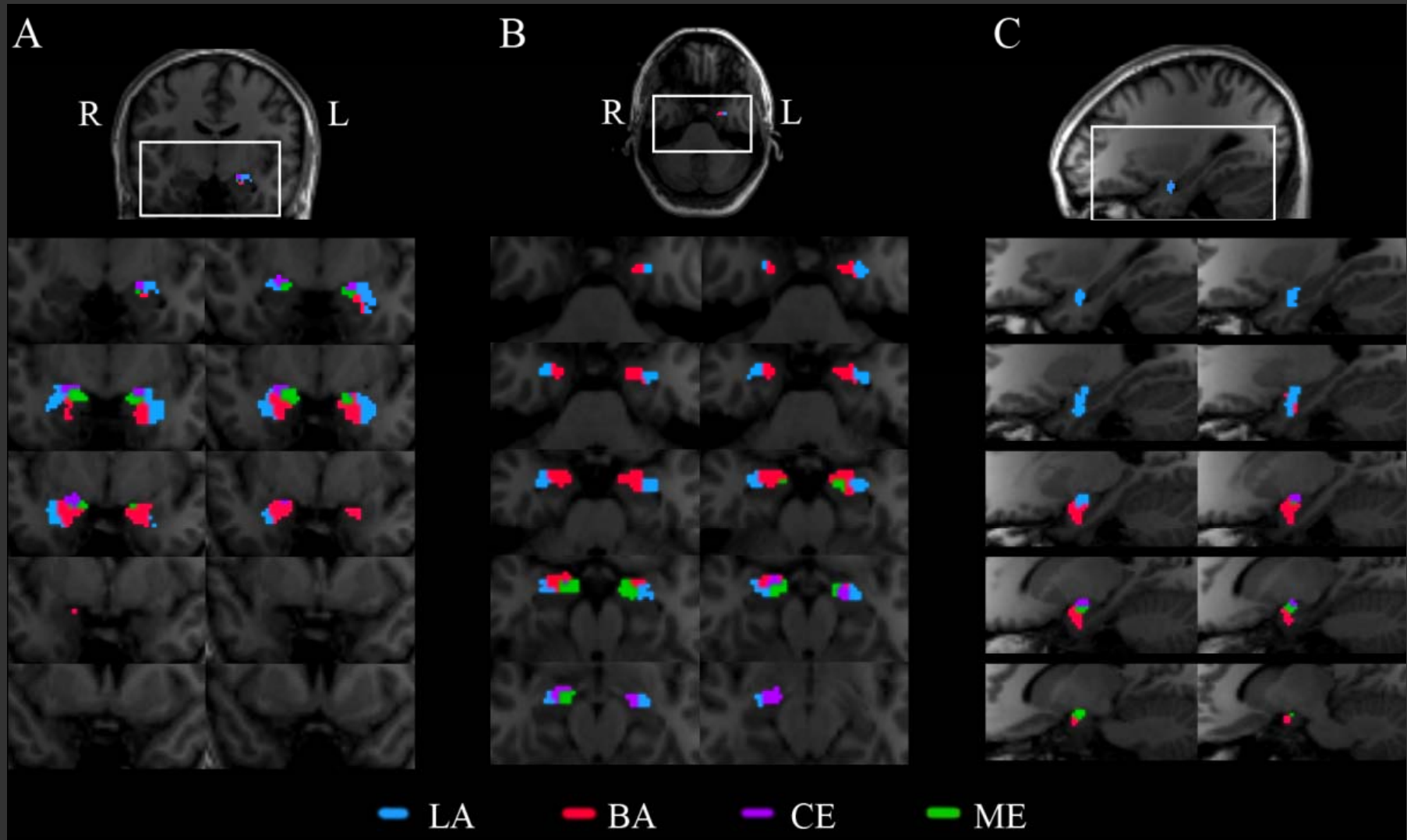
Work by Zeynep Saygin [zsaygin@mit.edu]

- Define nucleus groups based on summary of histological studies in rats, non-human primates, and humans

Target combinations	Putative nucleus
~(Superior parietal Post-central ¹⁻⁴ Medial orbitofrontal ^{1,2,5} Lateral occipital Pericalcarine Cuneus ⁶) & (Temporal pole Fusiform Lateral orbitofrontal & (Superior temporal Inferior Temporal ^{1-3,7-9})))	Lateral
(Parahippocampus ⁶ & (Hippocampus ^{15,16} Rostral anterior cingulate ^{6,17} Lateral orbitofrontal Medial orbitofrontal ^{18,23,5} Caudal middle-frontal Lateral occipital Pericalcarine Cuneus Lingual ^{6,19,20})) (Insula & (Accumbens Superior frontal ^{6,21-23}))	Basal
~(Brain Stem ^{10,11} & Ventral Diencephalon ^{6,12,13} & Thalamus Proper ¹⁴) & (Ventral Diencephalon ^{24,25} & (Striatum ⁵ Hippocampus ^{15,16}))	Medial
Brain Stem ^{10,11} & Ventral Diencephalon ^{6,12,13} & Thalamus Proper ¹⁴	Central
Table References <div> <div> 1. (Aggleton et al., 1980) 2. (Stefanacci and Amaral, 2000) 3. (Stefanacci and Amaral, 2002) 4. (Turner et al., 1980) 5. (Gloor, 1994) 6. (Amaral and Price, 1984) 7. (Kosmal et al., 1997) 8. (Yukie, 2002) 9. (Bachevalier et al., 1997) 10. (Price and Amaral, 1981) 11. (Price, 1981) 12. (Amaral et al., 1982) 13. (Mehler, 1980) </div> <div> 14. (Amaral et al., 1992) 15. (Aggleton, 1986) 16. (Amaral, 1986) 17. (Vogt and Pandya, 1987) 18. (Carmichael and Price, 1995) 19. (Amaral et al., 2003) 20. (Freese and Amaral, 2005) 21. (Barbas and De Olmos, 1990) 22. (Ghashghaei and Barbas, 2002) 23. (Russchen et al., 1985) 24. (Price, 1986) 25. (Price et al., 1987) </div> </div>	
Legend ~ NOT OR & AND	

Example subject

Work by Zeynep Saygin [zsaygin@mit.edu]



Manual vs. tractographic segmentation

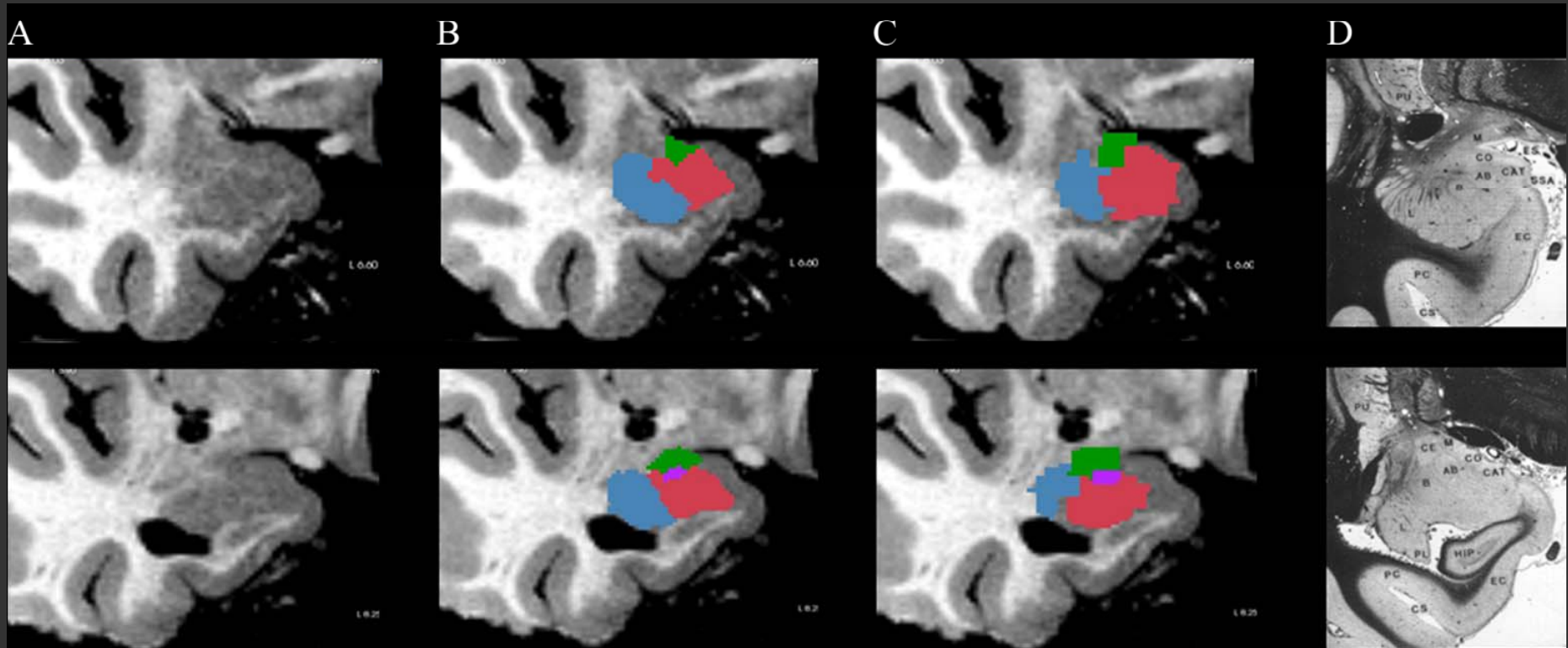
Work by Zeynep Saygin [zsaygin@mit.edu]

High-resolution

Manual seg.

Tractographic seg.

Example histo.

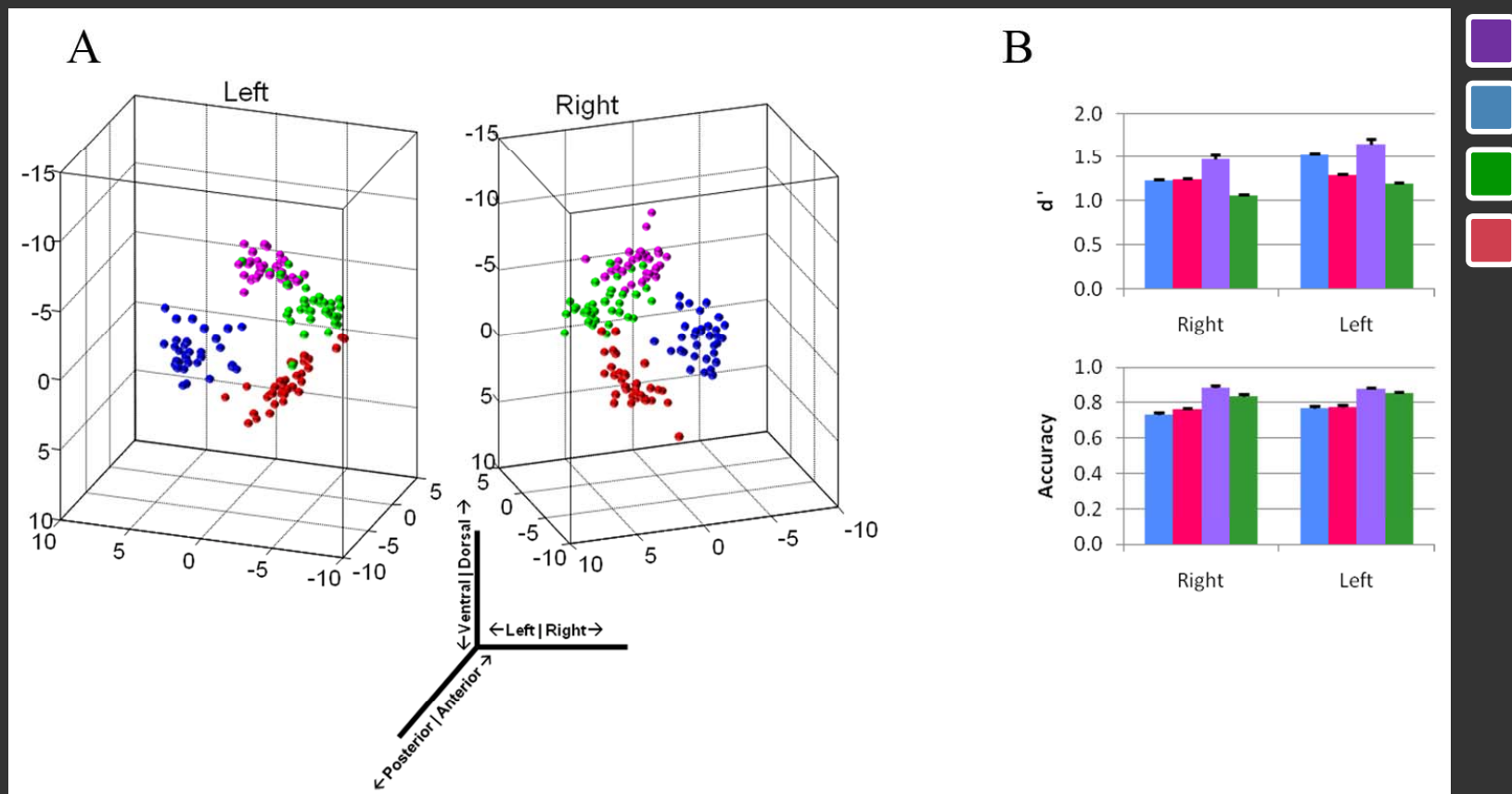


Dual-echo 20° flip angle
 $TE_0/TE_1/TR = 5\text{ms}/12\text{ms}/20\text{ms}$
600 μm isotropic
8 runs averaged ≈ 2 hrs

Inter-subject consistency

Work by Zeynep Saygin [zsaygin@mit.edu]

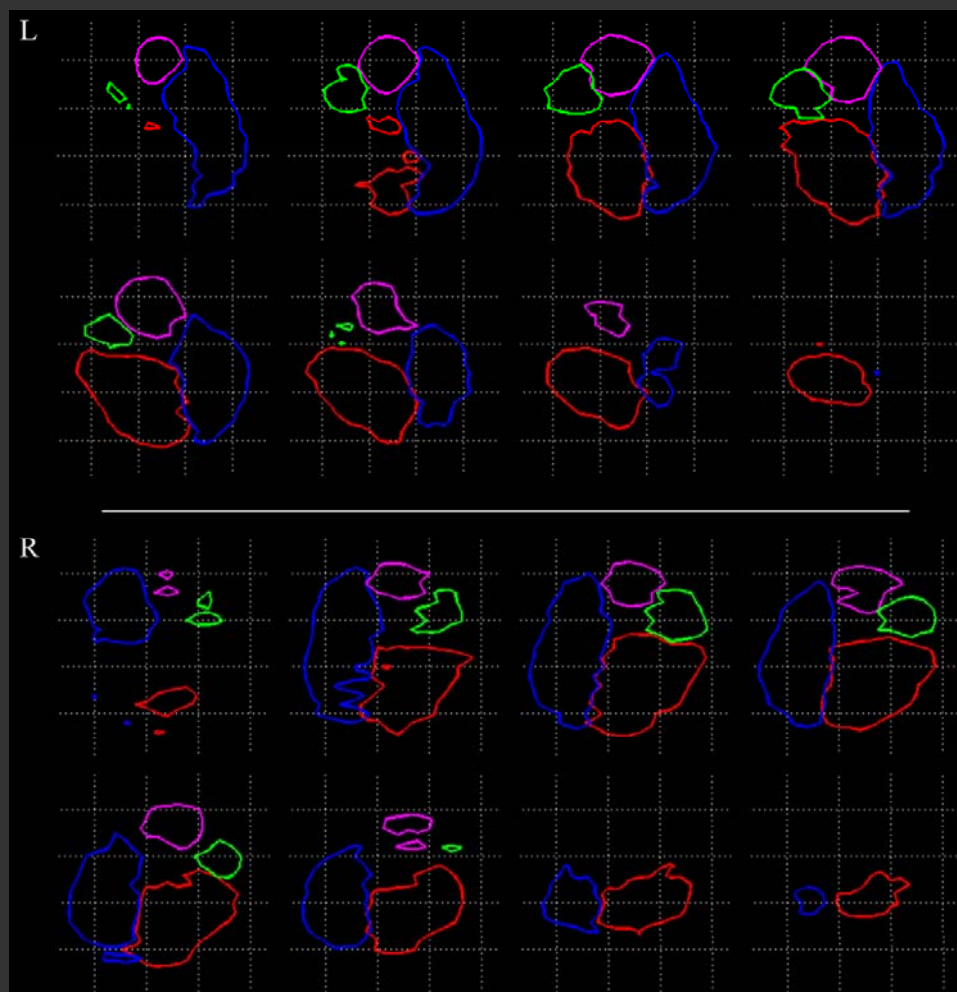
Tractographic segmentation results consistent across individuals



Group probability maps

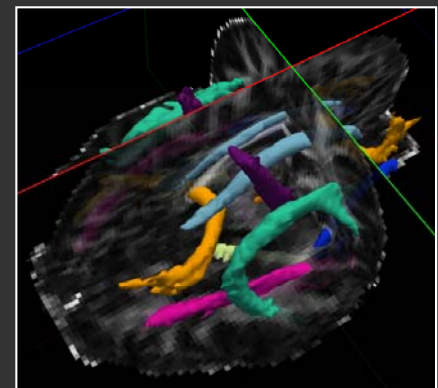
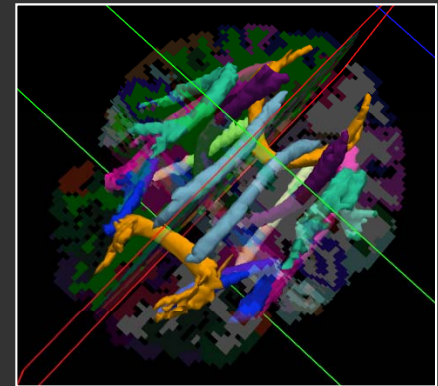
Work by Zeynep Saygin [zsaygin@mit.edu]

Group probability maps of tractographic segmentation labels, thresholded at $\geq 15/35$ subjects

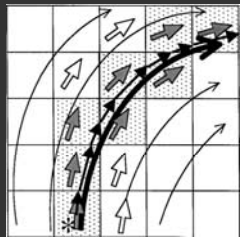


Automated tractography

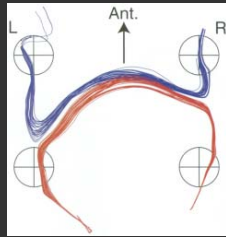
- **TR**Acts **C**onstrained by **U**nder**L**ying **A**natomy (**TRACULA**)
- Automatic reconstruction of probabilistic distributions of 18 major white-matter pathways
- No manual labeling of ROIs needed
- Use prior information on pathway anatomy from training data:
 - Manually labeled pathways in training subjects
 - FreeSurfer segmentations of same subjects
 - Learn neighboring anatomical labels along pathway
- Beta version available in FreeSurfer 5.1



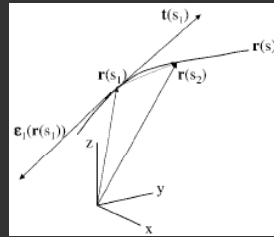
Many options for tractography!



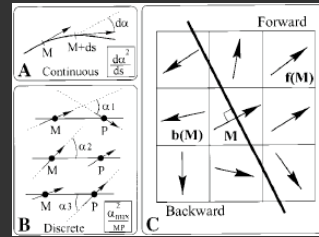
Mori '99



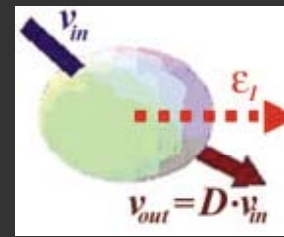
Conturo '99



Bassar '00

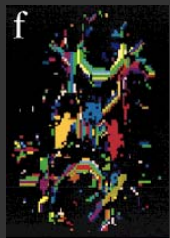


Poupon '00

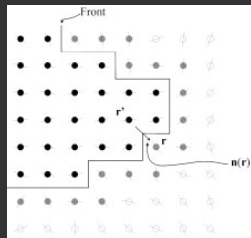


Lazar '03

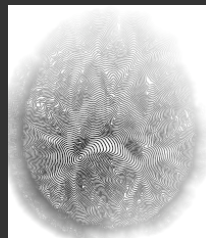
Some type of user interaction is typically needed to identify specific pathways (ROIs, bending angle thresholds, etc.)



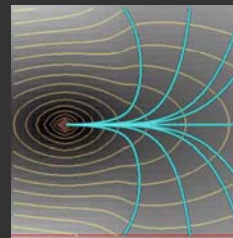
Jones '99



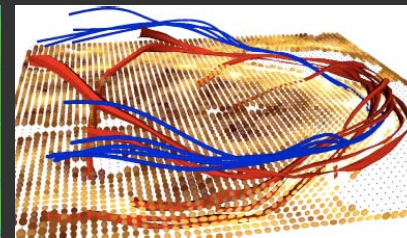
Parker '02



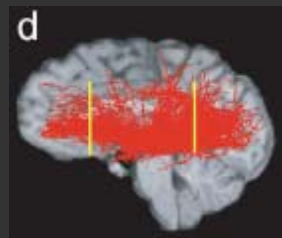
O'Donnel '02



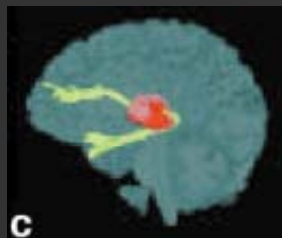
Jackowski '05



Pichon '05



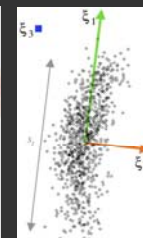
Hagmann '03



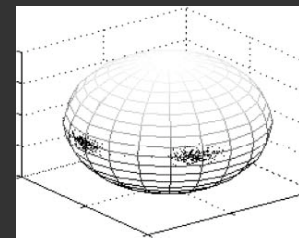
Behrens '03



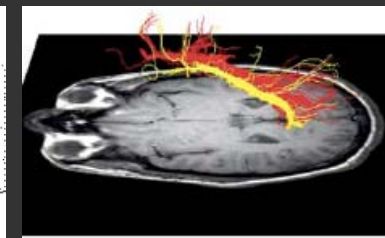
Jones '05



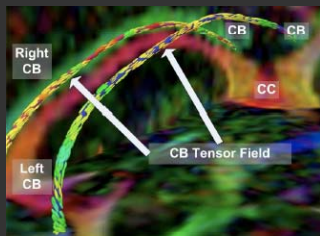
Lazar '05



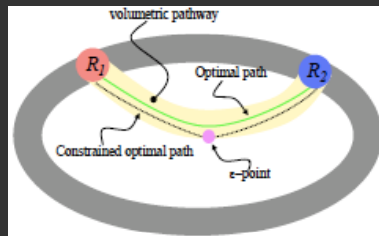
Parker '05



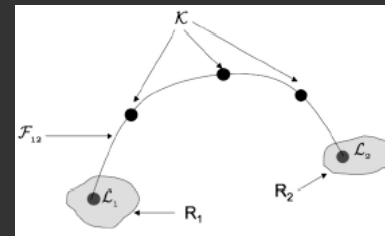
Friman '06



Melonakos '07

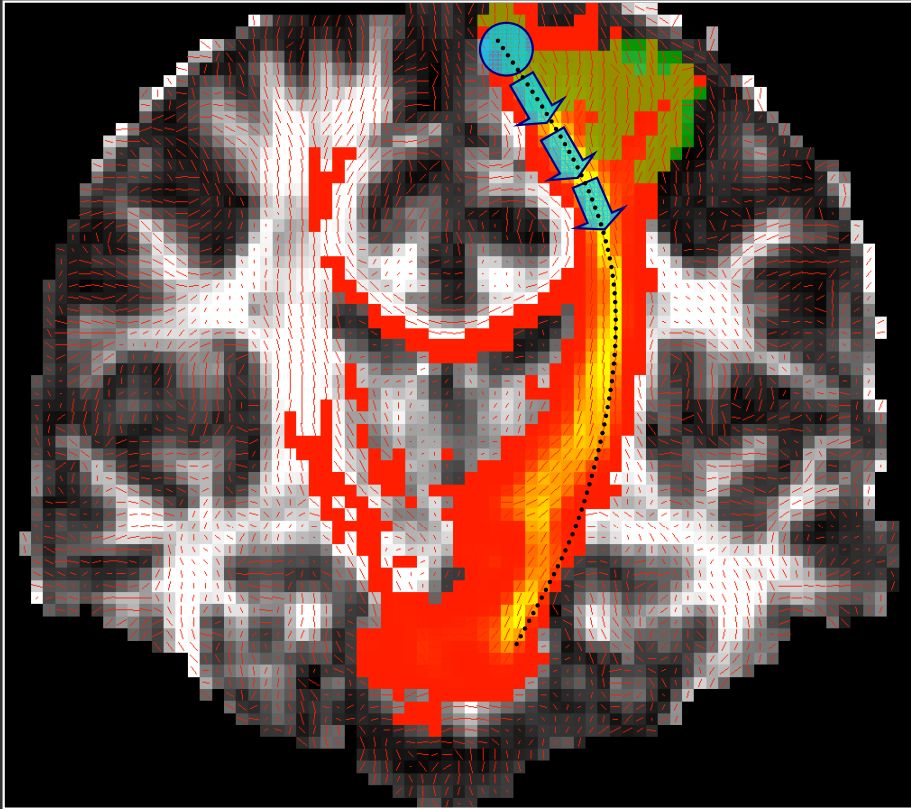


Fletcher '07



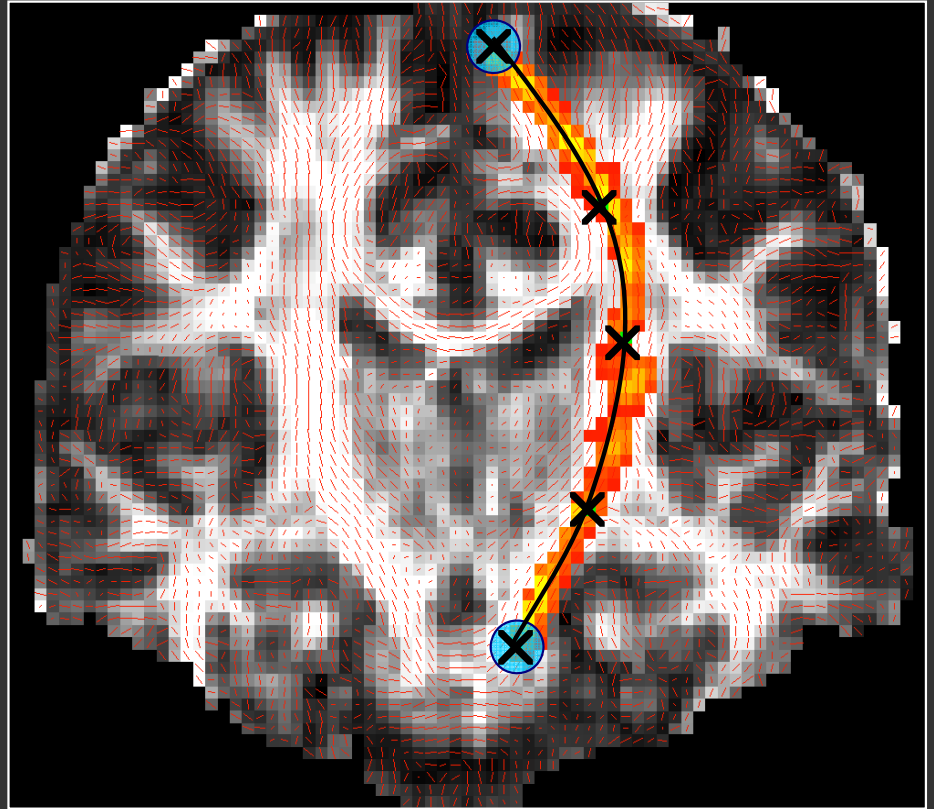
Jbabdi '07

Local vs. global tractography



Local tractography:

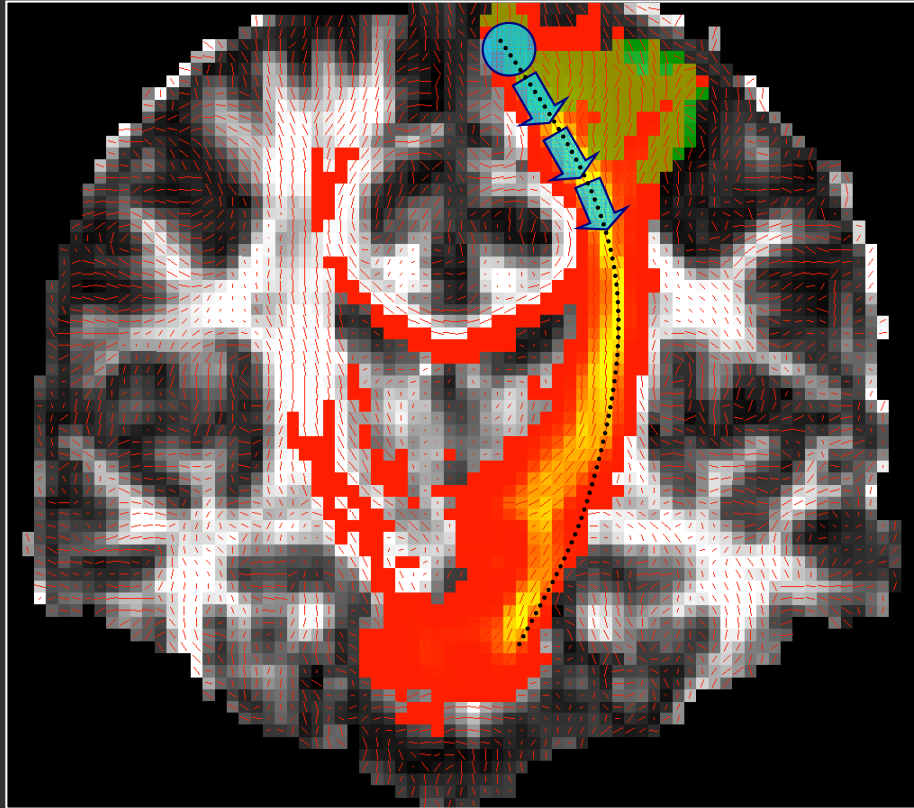
Fits pathway step-by-step, using local diffusion orientation at each step



Global tractography:

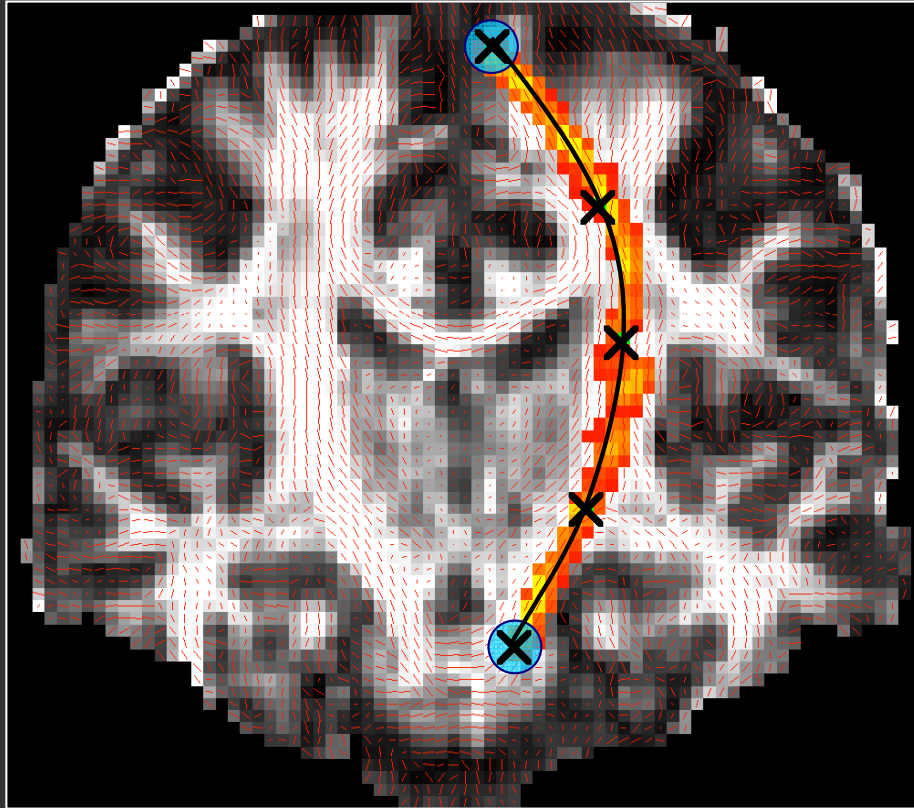
Fits the entire pathway, using diffusion orientation at all voxels along pathway length

Local tractography



- Best suited for exploratory study of connections
 - All connections from a seed region, not constrained to a specific target region
 - How do we isolate a specific white-matter pathway?
 - Thresholding?
 - Intermediate ROIs?
 - Non-dominant connections are hard to reconstruct
-
- Results are not symmetric between “seed” and “target” regions
 - Sensitive to areas of high local uncertainty in orientation (*e.g.*, pathway crossings), errors propagate from those areas

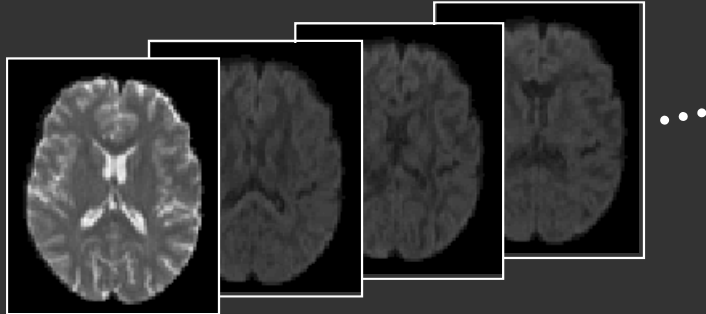
Global tractography



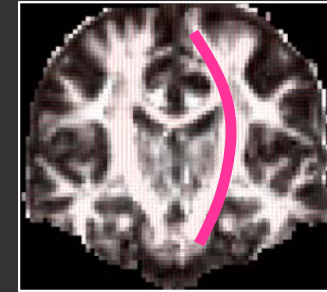
- Best suited for reconstruction of known white-matter pathways
 - Constrained to connection of two specific end regions
 - Not sensitive to areas of high local uncertainty in orientation, integrates over entire pathway
 - Symmetric between “seed” and “target” regions
- Need to search through a large solution space of all possible connections between two regions:
 - Computationally expensive
 - Sensitive to initialization

Global probabilistic tractography

Have image data \mathbf{Y}



Want most probable path \mathbf{F}



- Determine the most probable path based on:
 - What the images tell us about the path
 - What we already know about the path
- Estimate posterior probability of path \mathbf{F} given images \mathbf{Y}

$$p(\mathbf{F} | \mathbf{Y}) / p(\mathbf{Y} | \mathbf{F}) \propto p(\mathbf{F})$$

- $p(\mathbf{Y} | \mathbf{F})$: Uncertainty due to imaging noise

Fit of pathway orientation to ball-and-stick model parameters

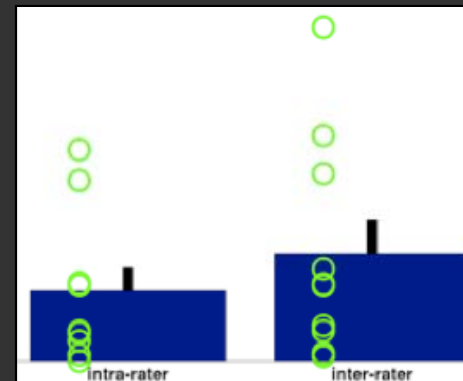
[Behrens '03, Jbabdi '07]

- $p(\mathbf{F})$: Uncertainty due to anatomical variability

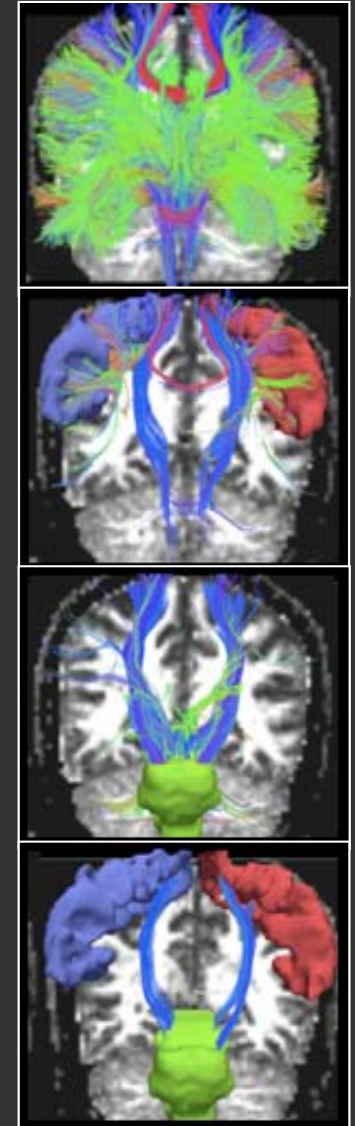
Fit of pathway to prior anatomical knowledge from training set

White-matter pathway atlas

- Labeling based on an established protocol [Wakana '07]
- Corticospinal tract
- Inferior longitudinal fasciculus
- Uncinate fasciculus
- Corpus callosum
 - Forceps major
 - Forceps minor
- Anterior thalamic radiation
- Cingulum
 - Cingulate (supracallosal)
 - Angular (infracallosal)
- Superior longitudinal fasciculus
 - Parietal
 - Temporal

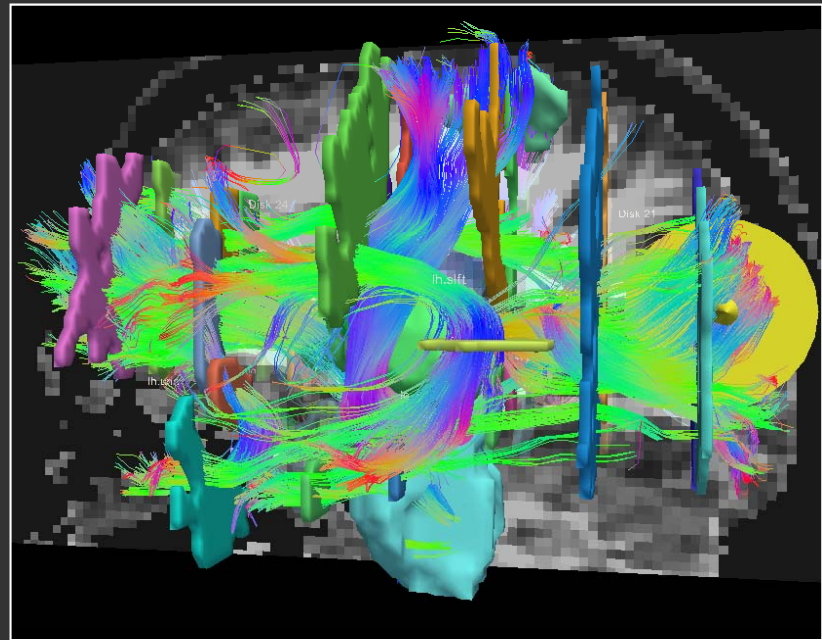
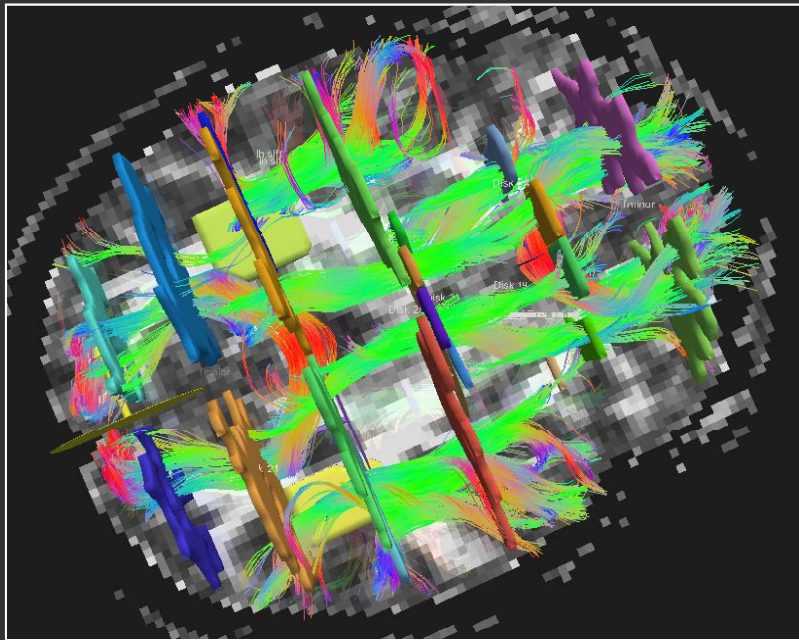


Intra/inter-rater errors:
1mm/2mm on average

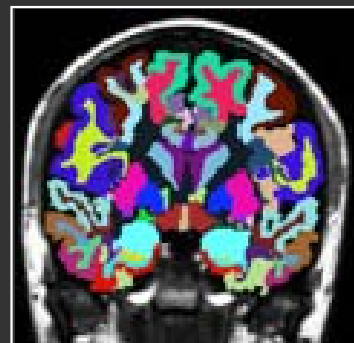


White-matter pathway atlas

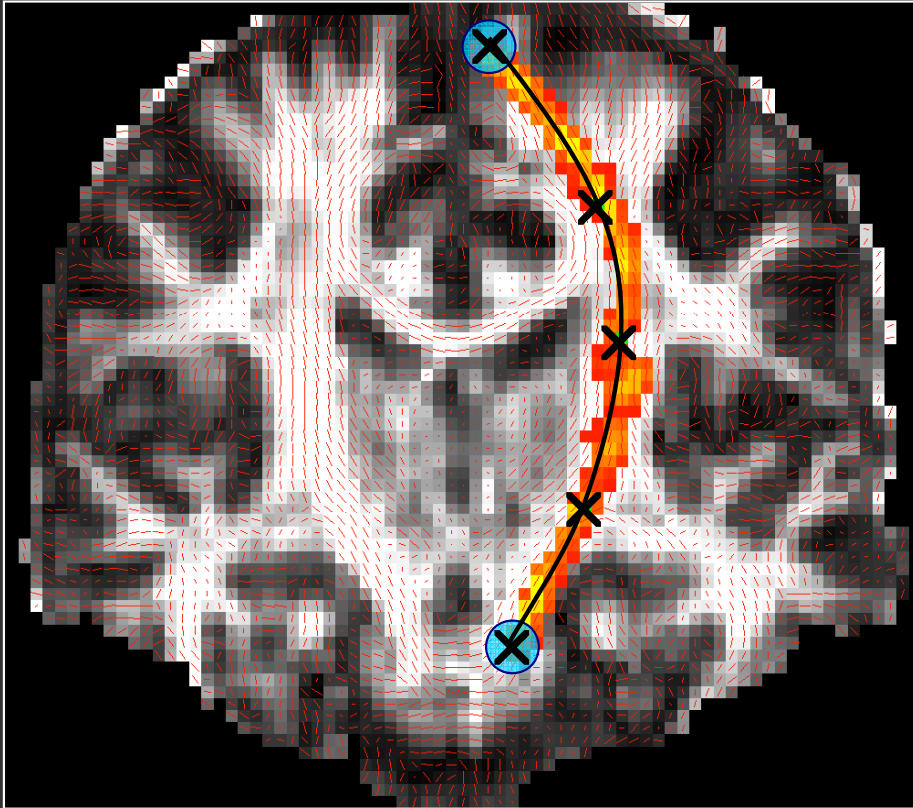
- **Manual labeling** of paths in training subjects performed in Trackvis



- **Anatomical segmentation maps** of training subjects from FreeSurfer



TRACULA outputs

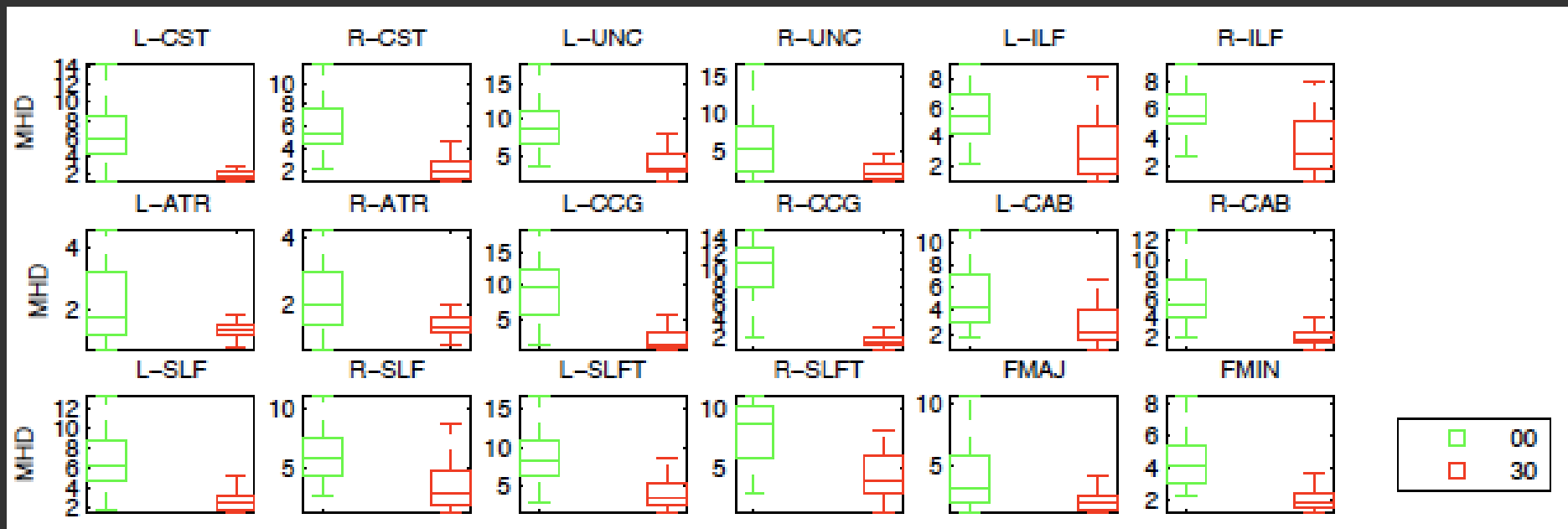


- Reconstruction outputs:
 - Posterior probability distribution of pathway given data (3D)
 - Maximum *a posteriori* (MAP) pathway (1D)
- Tract-based diffusion measures (FA, MD, RD, AD, etc):
 - Average over pathway distribution
 - Weighted average over pathway distribution
 - Average over MAP pathway
 - As a function of arc length along MAP pathway

Reliability in healthy subjects

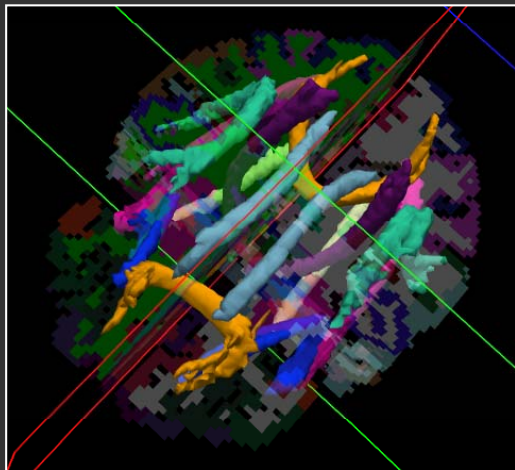
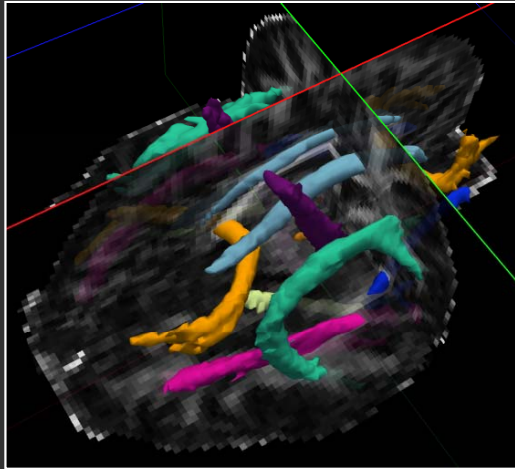
Data courtesy of Dr. Randy Gollub and MIND Institute

- Reconstruct pathways in 9 healthy subjects' test-retest data with
 - No training subjects
 - 30 of the remaining healthy subjects as training data
- Evaluate distance b/w automatically reconstructed MAP pathway from the test and retest scan



Schizophrenia study

Data courtesy of Dr. Randy Gollub and MIND Institute



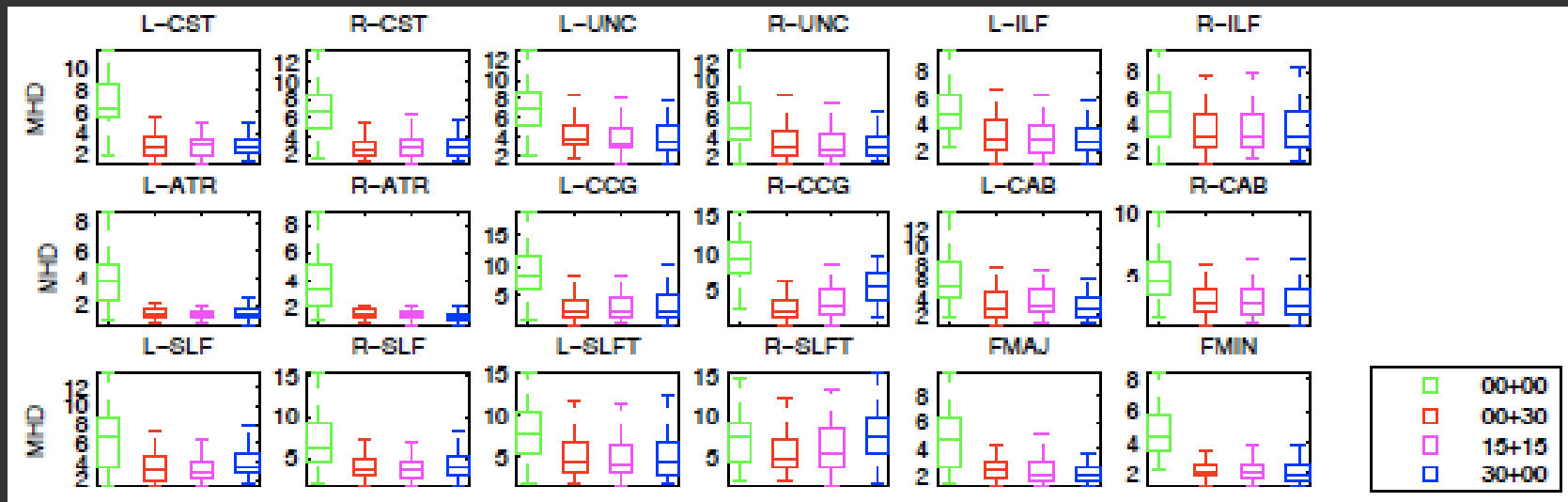
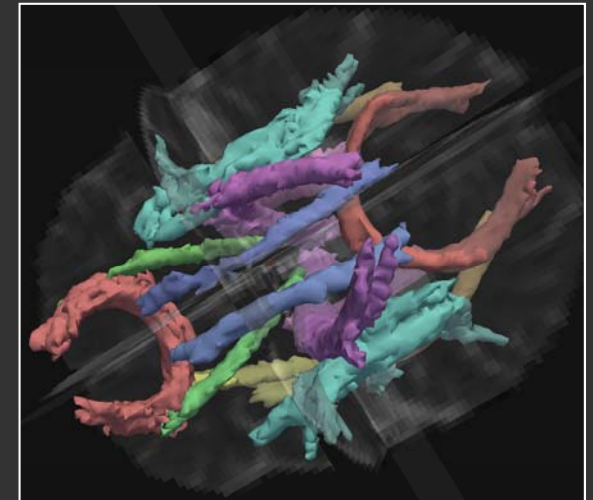
QuickTime™ and a
H.264 decompressor
are needed to see this picture.

Pathway distributions reconstructed automatically in a SZ patient
using 30 healthy training subjects

Schizophrenia study

Data courtesy of Dr. Randy Gollub and MIND Institute

- Reconstruct pathways in 34 SZ patients and 23 healthy controls with
 - No training subjects
 - 30 healthy training subjects
 - 15 healthy / 15 SZ training subjects
 - 30 SZ training subjects
- Evaluate distance b/w automatically reconstructed and manually labeled pathways



Acknowledgements

- Bruce Fischl
- Saad Jbabdi
- Tim Behrens
- Allison Stevens
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- David Salat
- Ruopeng Wang
- Lilla Zöllei
- Patricia Panneck
- Priti Srinivasan
- Randy Gollub
- Zeynep Saygin



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